INSTITUTE OF PUBLIC HEALTH

COLLEGE OF MEDICINE AND HEALTH SCIENCES

UNIVERSITY OF GONDAR

A THESIS PROPOSAL SUBMITTED TO THE INSTITUTE OF PUBLIC HEALTH, COLLEGE OF MEDICINE AND HEALTH SCIENCES, UNIVERSITY OF GONDAR, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF PUBLIC HEALTH.

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Full title of the research project	Incidence and Predictors of Tuberculosis among people living with HIV attending adult HIV care clinic at University of Gondar Referral Hospital, Northwest Ethiopia.
Duration of the project	February to May, 2012
Study area	University of Gondar Referral Hospital, North Gondar Administrative Zone, Amhara Region, Ethiopia.
Total cost of the project	15,788.30 Ethiopian Birr
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ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
CPT	Co-trimoxazole Prophylactic Therapy
EC	Ethiopian Calendar
EPTB	Extra Pulmonary Tuberculosis
HIV	Human Immunodeficiency Virus
ICF	Intensify Case Finding
IQR	Inter Quartile Range
IRIS	Immune Reconstitution Inflammatory Syndrome
MTB	Mycobacterium Tuberculosis
PLHIV	People Living with Human Immunodeficiency Virus
TB	Tuberculosis

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SUMMARY

Introduction: Tuberculosis (TB) is the commonest cause of morbidity and mortality among people living with human immunodeficiency virus (PLHIV). At least one in four deaths among people living with HIV can be attributed to TB, and many of these deaths occur in developing countries. Ethiopia is one of the highly affected countries by the TB/HIV co-infection epidemic. But there is no study conducted regarding the probabilities of developing TB and the potential predictors among HIV patients in the study area.

Objective: the aim of this study is to assess incidence of Tuberculosis and Predictors among people living with HIV attending adult HIV care clinic at University of Gondar Referral Hospital.

Methods: Institution based retrospective follow up study will be conducted at University of Gondar Referral Hospital Adult HIV care clinic. All 1838, patients above the age of 15 who were newly enrolled in HIV care clinic from October, 2006 to December, 2007 will be included. The study subjects will be followed retrospectively for five years (until December 31, 2011). The data will be entered to EPI- INFO version 3.6.1 then export to STATA 11for analysis. Kaplar-meier will be used for analysis of probabilities of developing TB. Log rank tests will be used to compare survival curves between the different categories of the explanatory variables. Both bivariate and multivariate Cox proportional hazards model will be fitted to identify the predictors. The necessary assumption of Cox proportional hazard model will be checked by using schoenfield residuals test.

Budget and work plan- The research will be conducted from February to April, 2012 and a total of **15,788.30** Birr is required to carry out this study.

1. INTRODUCTION

1.1. Statement of the problem

Tuberculosis (TB) is the most frequently diagnosed opportunistic infection and disease in human immunodeficiency virus (HIV) infected patients world-wide (1, 2). Despite being preventable and curable, it is still a leading killer of people living with HIV. At least one in four deaths among people living with HIV can be attributed to TB, and many of these deaths occur in developing countries (3). Worldwide about 11.1 million adults are co-infected with TB and HIV. Seventy percent of co-infected people are living in sub-Saharan Africa (4). An especial important aspect of the public health impact of HIV/AIDS has been the secondary epidemic of TB, most severe in area where rates of HIV infection are highest (5).

Globally, just over one in ten of the almost 9 million people who develop TB each year are HIV-positive; Of the 8.8 million incident cases in 2010, 1.1 million [1.0 million– 1.2 million] were among people living with HIV. The proportion of TB cases co infected with HIV is highest in countries in the African Region; overall, accounted for 82% of TB cases among people living with HIV. Globally in 2010, there were an estimated 0.35 million deaths from TB among people who were HIV-positive(6).

In the year 2009, TB is estimated that globally there were 9.4 million incident TB cases and there were 1.3 million TB deaths. The incidence rate, prevalence rate and mortality rate due to TB is highest in Africa. TB-HIV co-infection and drug resistant tuberculosis aggravate the TB situation globally. Of the 9.4 million incident cases in 2009, an estimated 1.1 million (12%) were HIV-positive. Of these HIV positive cases, 78% were in African (7).

The principal reason for the resurgence of TB in Africa is not the deterioration of control programs. Rather, it is the link between TB and HIV/AIDS. People who are latently infected with *Mycobacterium tuberculosis*—about one-third of the inhabitants of Sub-Saharan Africa are at hugely greater risk of developing active TB if they are also immunologically weakened by a concurrent HIV infection (8).

TB is one of the conditions associated with HIV infection for which cure is possible with appropriate therapy but untreated TB can accelerate the course of HIV infection. In an individual infected with HIV, the presence of TB may affect in many ways. TB increase HIV replication, which leads to increased viral load. These result in more rapid progression of HIV diseases. TB increases the occurrence of other opportunistic infections. It is also harder to diagnose in someone infected with HIV because the clinical manifestations of TB in HIV-infected patients are quite varied and generally show differently. One third of all people living with HIV worldwide are latently infected with Mycobacterium tuberculosis (MTB), making them 21-34 times more likely to develop active TB disease than people who are HIV negative (9-11).

The management of TB and HIV co-infected individual is challenging because of: pill burden(12) increase adverse effect(13), drug to drug interaction (14) and immune reconstitution inflammatory syndrome (IRIS) (15) due to this TB become the number one cause of mortality among people living with HIV (PLHIV). Late TB diagnosis contributes to increased death rates in PLHIV (4).

In Ethiopia, TB/HIV co-infected patients had greater risk of common mental disorders, lower quality of life, low family income and poor physical health than HIV infected patients without active TB (16, 17). Ethiopia ranks seventh among the world's 22 high-burden tuberculosis countries. It is also one of the highly affected countries by the TB/HIV co-infection epidemic. According to the World Health Organization's (WHO's) Global TB Report 2009, the country had an estimated 314,267 TB cases in 2007, with an estimated incidence rate of 378 cases per 100,000 population. The number of TB cases is likely to increase as Ethiopia's HIV/AIDS epidemic expands; while 16 percent of notified TB patients tested for HIV, 40 percent are HIV positive. Hence, the concomitant epidemics of HIV and tuberculosis are a major public health problem in Ethiopia; a TB/HIV collaborative program was launched since 2002 prior to WHO recommendation (2004)(18, 19).

1.2. Literature review

Different studies have documented the increased risk for TB among HIV-infected adults. According to a Taiwan short Report in 2009, the incidence rate of TB/ HIV co-infection among HIV cases varies during pre-free HAART era and post-free HAART era. It rose from 1.90% to 3.82% during 1993 to 1998 and decreased from 3.82% to 0.94% during 1998 to 2006. This study showed that Highly active antiretroviral therapy decreased the incidence rate of new TB/HIV co-infection cases among HIV cases and increased the survival rate of TB/HIV co-infection cases from 62.16% during the pre-free HAART era to 86.60% during post-free HAART era(20).

A cohorts study in the United States and Canada on 37 845 persons infected with HIV who initiated HAART revealed that 0.4% were diagnosed with tuberculosis after HAART. From This study, black race and baseline CD4 T lymphocyte count <200 cells/mm3 Were among the independent risk factors associated with tuberculosis diagnosis after HAART initiation(21). Another study showed that the majority of TB/ HIV co-infection were common in young adults (median age 34.7 years, IQR 30.1–40.3) and black Africans(22).

The use of both IPT and ART in HIV-infected patients significantly reduced tuberculosis incidence. retrospective medical record review in 11 026 HIV-infected patients receiving medical care at 29 public clinics in Rio de Janeiro, Brazil, showed that The overall tuberculosis incidence was 2.28 cases/100 person-years. Among patients who received neither ART nor IPT, incidence was 4.01/100 PY. Patients who received ART had an incidence of 1.90/100 PY and those treated with IPT had a rate of 1.27/100 PY. The incidence among patients who received ART and IPT was 0.80/100 PY. Multivariate Cox proportional hazards modeling revealed a 76% reduction in tuberculosis risk among patients receiving both ART and IPT (23).

In a ten years prospective study done in West Africa among 368 HIV- 1 infected adults the incidence rate of tuberculosis was 3.8/100 person-year. And it was diagnosed a median of 5.4 [interquartile range (IQR), 1.9–23.1] months after HIV diagnosis. The majority of those with incident TB (86.8%) had pulmonary TB.

The Incidence was highest in the group with low CD4 cell count, <200 10^6 cells/l. and with older age(24).

Results from placebo-controlled trial of 93 subjects in Dar es Salaam, Tanzania, among HIV-Infected Ambulatory Subjects found that Clinical and subclinical tuberculosis are common among ambulatory HIV-infected persons, and active tuberculosis was 15% of them 71% had clinical tuberculosis (symptoms or chest radiograph findings), and 29% had subclinical tuberculosis (positive sputum AFB stain or culture results but no symptoms or chest radiograph findings)(25). Another randomized control trial done in south Africa on adults living with HIV suggest that more widespread use of isoniazid preventive therapy is essential to control the epidemic of HIV related tuberculosis (26).

A cross sectional study conducted at Haydom Lutheran Hospital in northern rural Tanzania among 233 HIV/AIDS patients with age of 10 years and above revealed a high prevalence of tuberculosis (8.5%). Tuberculosis can occur at any stage of CD4+T cells depletion(27)

Another, Cross sectional record review on 1320 HIV/AIDS patients in Aminu Kano Teaching Hospital, Northern Nigeria 10.5% were co infected with TB (95% CI, 8.9% to 12.2%). Pulmonary TB was diagnosed in 74.6% patients, among whom only 17.5% were sputum-positive. The highest prevalence of TB, 13.7% (*n* = 28), was seen among patients aged 41–50 years. TB co infection was significantly associated with marital status, WHO clinical stage and CD4 count (28).

Results from a multi-centered cohort study in 8 Sub-Saharan African countries on 30,134 adult showed that the incidence of tuberculosis was 10.5 per 100 person years during the pre-ART and 5.4 during the ART period. For all types of tuberculosis, incidence was similar in the pre-ART period and initial 3 months of ART but declined over time receiving ART (from 13 per 100 person-years in the first 3 months to 1.5 per 100 person-years after 12 months of therapy). It also showed that throughout the follow-up period, rates of pulmonary tuberculosis remained 2-fold to 3-fold higher than extra pulmonary tuberculosis rates. Incidence was lower in rural sites, women, patients without prior history of tuberculosis, body mass index $\geq$ 18.5

kg/m2, and ≥ 200 nadir CD4 cells per microliter. The recurrence rate was 1.7 per 100 person-years (29).

The risk of developing tuberculosis among persons infected with HIV has been reported to be extremely high in the first 3 months after initiation of highly active antiretroviral therapy (HAART), with rates ranging from 1300 to 1700 per 100 000 person-years in developed countries and from 10 700 to 23 000 per 100 000 person years in developing countries (30, 31)

Evidence from, Prospective observational study in Mulago Hospital, Uganda; showed that Female sex (adjusted hazard ratio [aHR], 1.4) and baseline BMI ≤ 20 (aHR 1.9) predicted incident of TB in TB-HIV co-infections among patients with and without ART(32).

Ethiopia is one of the high burden tuberculosis countries. A retrospective review from five high burden tuberculosis countries revealed that in a very high TB burden countries incidence rates of TB among individuals on HAART is higher(Malawi , 14.3/100 person-years and Kenya, 17.6/100 person-years) as compared to low TB burden countries (33).

In a cohort of 185 pre-HAART and 180 HAART HIV patients done in Ethiopia the incidence rate of tuberculosis was 11.1 per 100 PYO (9 cases per 80.9 PYO) and 3.7 per 100 PYO (6 cases per 162.2 PYO) respectively. The median time to the diagnosis of tuberculosis in HAART cohort was 32 weeks (IQR, 14–56). The result showed that Tuberculosis incidence rate was lower in the HAART group. History of easy fatigability and prolonged fever predicted tuberculosis in the pre-HAART group but not in the HAART group (34). In another retrospective study done among 300 PLHIV attending an HIV care clinic in Dil Chora Referral Hospital, Ethiopia, during a 12-month period showed that 11% patients were diagnosed with TB, of whom 79% were identified in the first 6 months. And 15%of TB cases were smear-positive PTB while 53% were smear-negative PTB with 17% extra pulmonary TB (EPTB) (35).

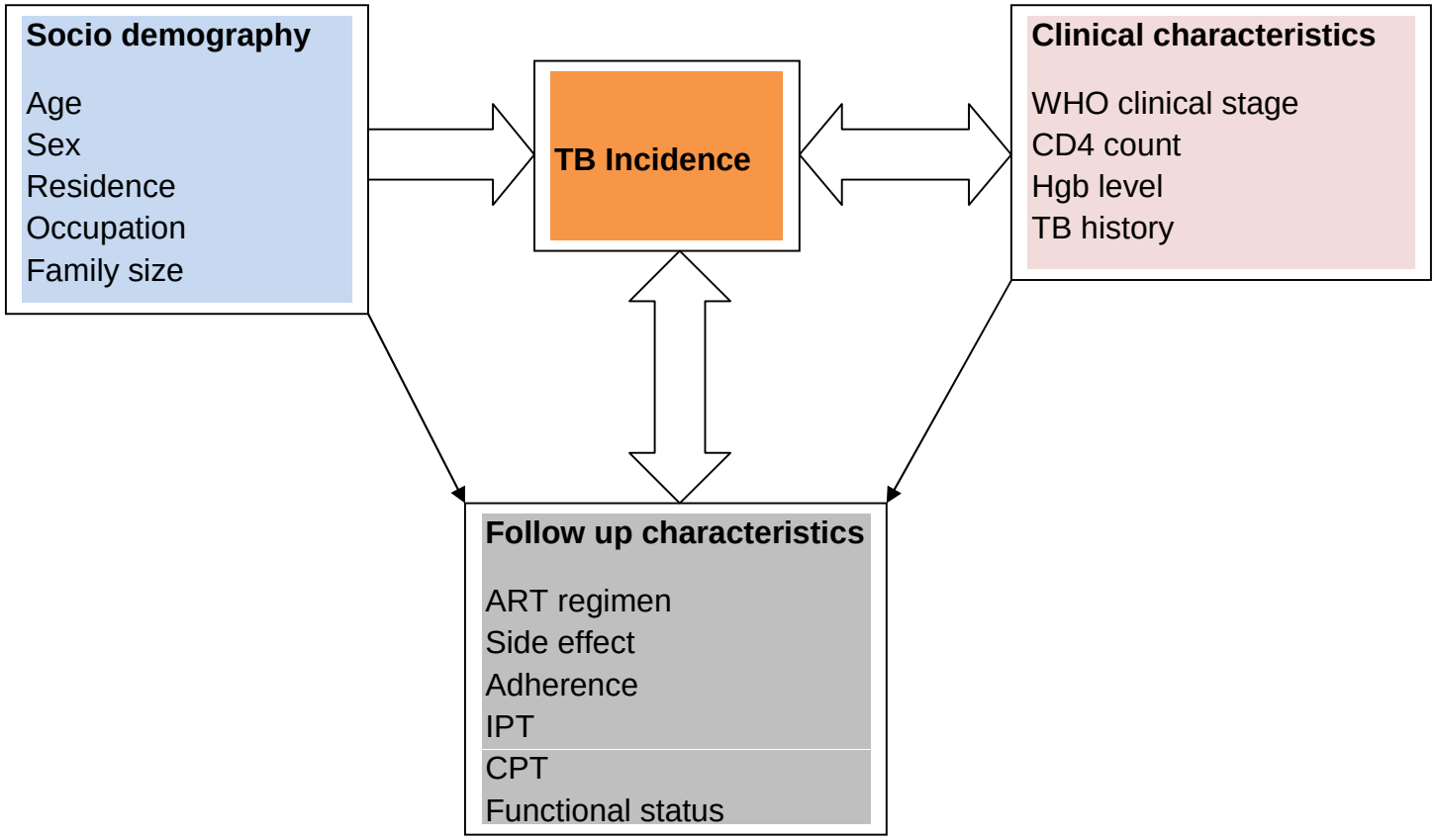

Fig. 1 Conceptual frame work which shows the occurrence of tuberculosis among HIV patients.

1.3. Justification of the study

Tuberculosis is the commonest cause of morbidity and mortality among PLHIV. It is also special in HIV infected patient because it increases the occurrence of other opportunistic infections and it occurs at various WHO clinical stage of HIV infection. In addition to this; unless we prevent in advance by identifying the potential risk factors, the anti TB treatment takes a long time unlike other OI's treatment which create pill burden for those who are on HAART.

In recent years, great efforts have been made to integrate tuberculosis diagnosis and treatment into HIV care which are essential to prevent, diagnose and treat TB among people with HIV and HIV among TB patients. This has created the need for additional research for better understanding of factors associated with incident tuberculosis which could help to improve service provision.

In University of Gondar Referral Hospital there are about 6444 and 3888 who ever stared and currently on ART respectively. However; the TB incidence rate and associated factors for TB are not studied yet. Therefore, this study will be important to show the incidence rate of TB in adult living with HIV and the possible predictors of the disease that can be addressed to reduce the occurrence of Tuberculosis among HIV patients.

2. OJECTIVE

2.1. General objective

- To assess incidence and Predictors of Tuberculosis among adults living with HIV attending HIV care clinic at University of Gondar Referral Hospital.

2.2. Specific objectives

- To determine incidence rate of Tuberculosis among adults living with HIV attending HIV care clinic at University of Gondar Referral Hospital.
- To identify the predictors of Tuberculosis among adults living with HIV attending HIV care clinic at University of Gondar Referral Hospital.

3. METHODS

3.1. Study design

A five years institution based retrospective follow up study will be conducted.

3.2. Study area and period

The study will be conducted at University of Gondar Referral Hospital HIV care clinic from February to April, 2012. It is located in North Gondar administrative zone, Amhara National Regional state, which is far from about 727 km Northwest of Addis Ababa (the capital city of Ethiopia). According to the 2007 population and housing census report , the total population size of Gondar town was estimated to be 206,987 (36). This Town is experiencing fast growth and according to the Gondar Town Health office report currently it has 209,163 populations(37). Currently Gondar town has one referral hospital and five government health centers. University of Gondar Referral Hospital is a teaching Hospital which serves more than five million people of the North Gondar zone and peoples of the neighboring zones. The HIV care services of the Hospitals were initiated in 2005 and have three clinics: Adult ART clinic, Pediatric ART clinic, and VCT clinic. The clinic has two medical doctors providing ART services, 1 MPH in reproductive Health, 2 Health officers , 2 BSc and 4 Diploma nurses, 2 data clerks, 2 data base manager,1 porter, 2 janitors 3 case manager and 8 adherence supporters (people living with HIV). The hospital uses standardized monitoring and evaluation tools and the data collection and management process is well controlled and supported by electronic data back-up and processing. There were about 6444 and 3888 who ever stared and currently on ART respectively. There were about 1,838 adults newly enrolled in to chronic HIV care and support program in the year 2006/2007.

3.3. Source and Study Population

The source population is all Adults living with HIV in University of Gondar Referral Hospital HIV care clinic. The study population will be those Adults living with HIV who were newly enrolled in HIV care clinic from October, 2006 to December, 2007.

Inclusion and Exclusion Criteria

Inclusions:

- All PLHIV aged 15 years and above who were newly enrolled in to HIV care clinic from October, 2006 to December, 2007 and
- PLHIV on HIV care clinic follow up program who had at least six months of follow up in the hospital.

Exclusions:

- PLHIV on HIV care clinic who had incomplete base line information (like age, sex, residence, CD4 counts, haemoglobin level) in the records.

3.4. Sample size and sampling procedures

All people living with HIV who were registered from October, 2006 to December, 2007 in Adult HIV care clinic of the University of Gondar referral hospital will be included in the study and followed them for five years (until December 31, 2011).

All 1,838 adults who were newly enrolled to HIV care and support during 2006/2007 will be included in the study provided that they fulfill the inclusion criteria. This period is selected in order to have a nearest five year follow up study periods and more or less the facility started full implementation of standardized formats, documentation and recording system in regular manner since this period. This is critical as the study is based on secondary data and it is also important to make sure that important variable for the study should be available for all enrolled subjects in the study. The likelihood of obtaining complete information on the variables for the study is very high during this period.

3.5. Variables of the Study

3.5.1. **Dependent variable** of the study will be the **time of occurrence of tuberculosis** in adults living with HIV who are on care and support in the Hospital.

3.5.2. **Independent variables of the study:**

Socio-demographic characteristics: Age, Sex, Residence, Family size, Educational level and Occupation, substance abuse.

Baseline clinical characteristics: WHO clinical Stag, CD4 counts/ total lymphocyte count (TLC), Haemoglobin level (Hgb), Body mass index (BMI)

Follow-up clinical and treatment related characteristics: INH prophylaxis therapy (IPT)**,** co-trimoxazole Prophylactic therapy (CPT)**,** ART drug regimen, Adherence, Co-morbid conditions (other OIs), Prior history of tuberculosis, Functional status**,** Presence of drug side effect

3.6. Operational definitions

Events - New or incident TB, which is defined in this study as the occurrence of TB in people living with HIV any time after enrolled it to HIV care. The type of TB can be smear positive pulmonary, smear negative pulmonary, extra-pulmonary or disseminated tuberculosis as identified by signs and symptoms, laboratory and/or X-ray diagnosis.

Censored – the survival time is censored when the individual is lost, drop out, transfer out and died by other causes before the end of the study period and finished the period without developing the event.

Lost- patients missing their appointment for follow up or drug pick up at least for one to three months.

Drop out- patients missing their appointment for follow up or drug pick up for more than three months

Transferred out – those patients who are transferred to other health care facilities

Body Mass Index (BMI): is the ratio of weight to height in meters squared; And it will be classified as (38): <18.5 = Underweight, 18.5-24.9 = Normal weight, 25-29.9 = Overweight, 30 and above=Obese.

Adherence to ART: will be classified in to good, fair, and poor according to the percentage of drug dosage calculated from the total monthly dose of ART drugs. Which describe as **G**ood (equal to or greater than 95% or ≤ 3 doses missed per month), **F**air (85- 94% or 4-8 doses missed per month), or **P**oor (less than 85% or ≥ 9 doses missed per month)(39).

3.7. Data Collection Tools and Procedures

The available information on the patient records has been first observed and appropriate data extraction tool has been prepared in English. Using this format, staffs who are working on the HIV care clinic will collect the data on the already existing records.

3.8. Data quality control

Quality of data will be maintained by recruit staffs for the data collection who are working at the HIV care clinic. The data collectors and supervisor will be given intensive training for one day before the data collection on the objective of the study and how to retrieve data for this study purpose using the data extraction format. They will be briefed on the definition of variables on the questionnaires and registration charts. The data extraction tool will be pre-tested for consistency of understanding and completeness of data items on 25 charts at the same facility as it is a secondary data. The retrieval process will be closely monitored by the principal investigator and the supervisor throughout the data collection period. Completed questionnaires will be checked regularly for completeness of information and any gaps identifies will be immediately communicated to the data collectors. Double entry will be done on 10% of the questionnaires.

3.9. Data processing and analysis

After the data checked for its consistency and completeness, it will be entered to EPI- INFO version 3.6.1 then exported to STATA 11 for analysis. Data entry will be conducted by the principal investigator and it will be cleaned before analysis.

Descriptive and summary statistics will be carried out. Incidence density (ID) will be calculated for the entire study period. Kaplan-Meier plots will be used for analysis of probabilities of developing TB. Generalized log rank tests will be used to compare survival curves between the different categories of the explanatory variables.

Both bivariate and multi variate Cox proportional hazard model will be used to identify the predictors. Variables having p value up to 0.2 (20%) in the bivariate analysis will be fitted in to the multi variate model. Ninety five percent confidence interval of hazard ratio will be computed and variable having p value less than 0.05 in the multi variate cox proportional hazards model will be considered as significantly associated with the dependent variable. The necessary assumption of cox proportional hazard model will be checked by using schoenfield residuals test.

4. ETHICAL CONSIDERATION

Ethical clearance will be obtained from the Institution review board of University of Gondar, Institute of Public Health. Permission will be obtained from the Hospital's management and HIV care clinics focal person to use the secondary data for the purpose of this study. The name or any other identifying information will not be recorded on the questionnaire and all information taken from the chart will be kept strictly confidential and in a safe place. The information retrieved will only be used for the study purpose.

5. DISSEMINATION OF RESULTS

The final result of the study will be summated as partial fulfillment of the degree of Master of Public Health in epidemiology and biostatistics to the institute of Public Health, College of Medicine and Health Sciences, University of Gondar.

It will be disseminated to university of Gondar Referral Hospital, Amhara regional Health bureau, North Gondar Health Department and other governmental and none governmental organizations who are specially working on HIV/AIDS and Tuberculosis. The result will be also presented at University of Gondar annual research conference, Ethiopian Public Health Association Annual Conference and other conferences and workshops. Moreover, the result will be sent for publication at scientific National or international journals.

6. WORK PLAN

Activities	R	January				February				March				April				May				June			
Topic selection	PI																								
Topic defense	PI																								
Proposal preparation	PI																								
First draft proposal submission	PI																								
Proposal defense	PI																								
Final proposal submission	PI																								
Ethical clearance	RPO																								
Training of data clerk	PI																								
Pre test	PI,DC																								
Data collection & entry	DC,S																								
Data analysis & write up	PI																								
First draft submission	PI																								
Submission of final thesis	PI																								
Preparation for thesis defense	PI																								
Thesis defense	PI																								

NB: PI=Principal Investigator **DC=** Data Collector **S=**Supervisor **R=** Responsible body
RPO= Research Publication Office

7. COST OF THE RESEARCH PROJECT

Personnel costs						
Title	**Qualification**	**Number of personnel**	**Per dime**	**Duration (days)**	**Total cost**	Remark
Supervisors	Physician, BSc. Nurse or HO	1	70.00	18	1260.00	Training, pretest & data collection
data collectors	BSs nurse	4	58.00	18	4176.00	,,
data clerk	Diploma nurse	1	58.00	18	1044.00	,,
Data enter	MPH students	1	70.00	15	1050.00	Principal investigator
Data analysis	MPH students	1	70.00	15	1050.00	Principal investigator
secretary		1	58.00	10	580.00	
Total					**8104.00**	

Equipment and Supplies					
Equipment & Supplies	**Units**	**Quantity**	**Unit cost**	**Total cost**	
Paper	Rim	10	120.00	1200.00	
Stapler	Number	1	50.00	50.00	
Staples	Pack	2	10.00	20.00	
Eraser	Number	5	1.00	5.00	
Pen	Number	18	2.50	45.00	
Pencils	Number	18	.50	9.00	
Note book	Number	10	10.00	100.00	
Printing	Page	110	2.00	220.00	For the questionnaire, proposal and thesis
Duplication	Page	7000	0.50	3500.00	,,
Binding	Number	10	10.00	100.00	,,
Flash disc	Number	1	400.00	400.00	
CD-RW	Number	8	25.00	200.00	
Mobile cared	Number	3	100.00	300.00	For communication
packed water	Number	10	10.00	100.00	During training
Total				**6249.00**	

Budget summary		
1. Sub total cost for personnel	8104.00	
2. Sub total cost for materials and supplies	6249.00	
Total	14,353.00	
10% contingency	1435.30	
Grand total	**15788.30**	

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9. ANNEX

Annex 1 - information sheet

Title of the Research Project: Incidence of Tuberculosis and Predictors among HIV infected patients attending adult HIVcare clinic at University of Gondar Referral Hospital, Northwest Ethiopia.

Name of Investigator: Kefylalew Addis (Bsc in Public Health Officer)

Name of the Organization: University of Gondar College of Medicine and Health Sciences, Institute of Public Health.

Name of the Sponsor: University of Gondar

Introduction: this information sheet is prepared for University of Gondar Referral Hospital administration and Hospital HIV care clinic coordinating office. The aim of the form is to make the above concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: To determine incidence of Tuberculosis and its Predictors among adult living with HIV attending adult HIV care clinic at University of Gondar Referral Hospital.

Procedure: In order to achieve the above objective, information which is necessary for the study will be taken from HIV care medical record follow up forms.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from medical chart, it will not inflict any harm on the patients. The name or any other identifying information will not be recorded on the questionnaire and all information taken from the chart will be kept strictly confidential and in a safe place. The information retrieved will only be used for the study purpose.

Benefits: the research have no direct benefit for one whose document/ record is included in this research. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plan there is a benefit for clients in the program of getting

appropriate care and treatment services. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on HIV/TB collaborative program planning and management**.**

Confidentiality: to reassure confidentiality the data on the cart will be collected by those individuals who are working on the HIV care clinic in the facility and information will be collected without the name of the clients. The information collected from this research project will be kept confidential and will be stored in a file. In addition, it will not be revealed to anyone except the investigator and it will be kept in key and locked system with computer pass ward.

Person to contact: This research project will be reviewed and approved by the institutional review board of College of Medicine and Health Science, University of Gondar. If you want to know more information, you can contact the committee through the address below. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any time you want.

1. Kefyalew Addis, University of Gondar, College of Medicine and Health Science, Department of Health Officer: principal investigator
   Cell phone: +251- 09 20 25 66 99
   E-mail: kefadis@gmail.com
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3. Ansha Nega (RS, BSc, MSc) University of Gondar College of Medicine and Health sciences ,Department of Environmental and Occupational Health and safety: Advisor
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   E-mail: ains262000@gmail.com

የመረጃ እና ስምምነት ዉል ቅጽ

የምርምሩ/ጥናቱ ርዕስ ፡

በጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል የኤች አይ ቪ ክትትል ባላቸዉ አቂዎች ላይ ክትትል ከጀመሩ በኋላ ያለዉን የሳንባ ነቀርሳ ክስተት እና ተዛማጅ ምክንያቶችን በተመለከተ

የዋና ተመራማሪ ስም ፡ ከፍያለዉ አዲስ

የድርጅቱ ስም ፡- በጎንደር ዩኒቨርሲቲ ህክምናና ጤና ሳይንስ ኮሌጅ የህብረተሰብ ጤና

አጠባበቅ ተቋም

ወጭውን የሚሸፍነው አካል፡- ጎንደር ዩኒቨርሲቲ

መግቢያ፡

ይህ የመረጃ እና የስምምነት ዉል ቅጽ የተዘጋጀዉ ለጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል አስተዳደር እንዲሁም በሆስፒታሉ ለሚገኘዉ የኤች አይ ቪ ክሊኒክ ክትትል ሀላፊ ነዉ። ዋና አላማዉም ስለ ምርምሩ ዓላማ ፤ ስለ መረጃ አሰባሰቡ ፤ እንዲሁም ጥናቱን ለማካሄድ ፍቃድ ለማግኘት ከላይ የተጠቀሱት አካላት ግልጽ እንዲሆንላቸዉ ለማድረግ ነዉ።

ጥናቱ የሚካሄድበት ምክንያት፡

የዚህ ጥናት ዋና አላማ በጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል የኤች አይ ቪ ክትትል ባላቸዉ አቂዎች ላይ ክትትል ከጀመሩበት ጊዜ አንስቶ ያለዉን የሳንባ ነቀርሳ ክስተት እና ተዛማጅ ምክንያቶችን ለማጥናት ታቅዶ የተዘጋጀ ነዉ ።

አተገባበር

የጥናቱን አላማ ለማሳካት በጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል የኤች አይ ቪ ክትትል ባላቸዉ የአዋቂዎች ቻርት ላይ መረጃዉ ይሰመሰባል።

ሊገጥም የሚችል ችግር /አለመመቸት

የሚወሰደዉ መረጃ ሙሉ በሙሉ ከቻርት ላይ ብቻ ስለሆነ በበሽተኞች ላይ ምንም አይነት ጉዳት አያመጣም። የቻርቱ ባለቤት ስምና መለያ ቁጥር ከመጠይቁ ላይ አይገለጽም። በተጨማሪም የተሰበሰበዉ መረጃ በደንብ ተቆልፎ ይቀመጣል እንዲሁም ለታቀደለት አላማ ብቻ ይዉላል ።

ጥቅሞች

በዚህ ጥናት ተሳታፊ የሚሆኑ ሰዎች በቀጥታ ሊያገኙት የሚችሉት ጥቅም የለም ። ቢሆንም ግን መረጃቸዉ የኤች አይ ቪ ክትትል ባላቸዉ አቂዎች ላይ ክትትል ከጀመሩበት ጊዜ አንስቶ ያለዉን የሳንባ ነቀርሳ ክስተት እና ተዛማጅ ምክንያቶችን ለማጥናት ይጠቅማል። ከጥናቱ ዉጤት ተነስቶ በሚደረገዉ የፕሮግራም መሻሻል በቀጥታም ባይሆን ተጠቃሚ ይሆናሉ።

ሚስጥራዊነት

ለዚህ ጥናት የሚሰበሰበዉን መረጃ ሚስጥር ለመጠበቅ ሲባል መረጃዉ የሚሰበሰበዉ በሆስፒታሉ ዉስጥ በሚገኘዉ የኤች አይ ቪ ክሊኒክ በሚሰሩ ነርሶች ነዉ ። ከዚህ በኋላ የተመረጡት ነርሶች በቻርቱ ላይ የሚገኘዉን መረጃ ይሰበስባሉ ። የተሰበሰበዉ መረጃም ከጥናቱ ዋና ተመራማሪ እና ረዳቶቹ በስተቀር ለሌላ ለማንኛዉም ሰዉ ግልጽ አይሆንም ። የተገኘዉ መረጃም ለታቀደለት አላማም ብቻ ይዉላል።

ሊያገኙዋቸዉ የሚችሉ ሰዎች

የዚህ ምርምር ፕሮጀክት በጎንደር ዩንቨርሲቲ የስነ ምግባር ኮሚቴ ታይቶ የሚጸድቅ ይሆናል ። የትኛዉንም ዓይነት ጥያቄ መጠየቅ ቢፈልጉ ከዚህ ቀጥሉ የተጠቀሱትን ግለሰቦች ማግኘት እና በማንኛዉም ጊዜ መጠየቅ ይችላሉ ።

1. ከፍያለዉ አዲስ ፡- ጎንደር ዩንቨርሲቲ ፤ጤና መኮነን ትምህርት ክፍል ፤ዋና ተመራማሪ
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2. ዶ/ር በላይነዉ ዋሴ ፡- ጎንደር ዩንቨርሲቲ፤ ህብረተሰብ ጤና አጠባበቅ ተቋም
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Annex 2- Data collection tool

Questionnaire prepared for collection of data on the patients ART or/and pre ART medical registration book/chart to assess the incidence of Tuberculosis and Predictors among adult living with HIV attending adult HIV care clinic at University of Gondar Referral Hospital. **Code No.**_____

S. N.	Part I: Socio demographic characteristics		Skip to Qn
101	Date of enrolment	----------/---------/-------- DD/MM/YY	
102	Age at enrolment	---------- year	
103	Sex	1. Male 2. Female	
104	Marital status	1. Never married/ single 2. Married 3. Separated/ divorced 4. Widowed/er 5. Others (specify)----------	
105	Level of education	1. No education 2. Primary 3. Secondary 4. Tertiary 5. Not recorded	
106	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5. Others (specify) ----------	
107	Occupation	1. Employed 2. Unemployed 3. Not recorded	
108	Address	1. Urban 2. Rural 3. Not recorded	
109	Number of house hold	----------persons	
110	Disclosure status	1. Disclosed 2. Not disclosed	
111	Addictions/Substance abuse	1. Tobacco 2. Alcohol 3. drugs	
	Part II: Past Tuberculosis treatment history		
201	Did the patient had past TB treatment history?	1. Yes 3. Not recorded 2. No	2 or 3→ 301
202	Is the treatment completed?	1. Yes 2. No	
203	Date treatment started	-------/---------/-------- (DD/MM/YY)	
204	Date treatment completed	-------/---------/---------(DD/MM/YY)	
	Part III: HIV care/ ART follow up		
301	ART status	1. Pre-ART 2. ART	
302	Date confirmed HIV+	---------/------/------(DD/MM/YY)	
303	ART Eligible date	---------/------/------(DD/MM/YY)	
304	Eligible criteria	1. CD4 cell count 3. Both 2. WHO clinical stage 4. Not recorded	
305	Date ART started	---------/------/------(DD/MM/YY)	
307	Initial Regimen	1. D4T/3TC/NVP 2. ZDV/3TC/NVP 3. D4T/3TC/EFV	

		4. ZDV/3TC/EFV 5. Other (specify)----------	
308	Was the Regimen changed?	1. Yes 2. No	2→310
309	When was it changed	---------/------/------DD/MM/YY	
110	New regiment	1. First line 2. Second line	
311	Reason for switch	1. side effects 3. TB 2. Pregnancy 4. Others ----------	

Part IV: Follow up form to be filled

Months on ART	Outcome					Weight(kg)	Height (cm)	Functional status (W,A,B)	WHO stage	TB status	INH	OIs	CPT Adh (G,FP)	ART					CD4 count	Hgb
	Alive	Dead	Drop out	Transfer out	Stop									Adh (G,F,P)	why	Dispense	Side effect	Reason for change		
Initial																				
3																				
6																				
9																				
12																				
18																				
24																				
30																				
36																				
42																				
48																				
54																				
60																				
Last visit -------/------/------																				

If the patient Dead, drop out, transfer out or stop when was it occurs -----/-----/---DD/MM/YY?

401	Did the patient develop TB during follow up	a. Yes b. No	
402	When was it developed?	----------/----------/----------DD/MM/YY	
403	During what was it developed?	1. Pre ART 2. ART	
404	What type of TB was it?		

Name of data collectors ----------sign ----------date ----------

Approved by ----------sign ----------date ----------

Annex -3 dummy tables

Table 1: socio demographic characteristics of patients on chronic HIV care at University of Gondar Referral Hospital, from October, 2006 to December, 2007

Characteristics	Number	Frequency (%)	Total
Age			
15-29			
30-44			
≥45			
Sex			
Male			
Female			
Marital Status			
Never married			
Married			
Separated/divorced			
Widowed			
Religion			
Orthodox			
Muslim			
Protestant			
Catholic			
Others			
Educational status			
No education			
Primary			
Secondary			
Tertiary			
Not recorded			
Occupation			
Employed			
Unemployed			
Not recorded			
BMI			
Underweight			
Normal			
Overweight			
Obese			

Table 2: baseline clinical and immunological status of HIV patients on chronic HIV care at University of Gondar Referral Hospital, from October, 2006 to December, 2007

Characteristics	Frequency	Present (%)	Total
ART eligible criteria			
WHO clinical stage			
CD4 count			
Both			
WHO clinical stage at			
I-II			
III			
IV			
Initial regimen			
D4T/3TC/NVP			
ZDV/3TC/NVP			
D4T/3TC/EFV			
ZDV/3TC/EFV			
Others			
Regimen change during follow up			
Yes			
No			
Developed side effect for ART			
Yes			
No			
IPT provided			
Yes			
No			
CPT provided			
Yes			
No			
past TB treatment history			
Yes			
No			
regimen switched to 2nd line			
Yes			
No			

Table 3: Tuberculosis incidence density rate stratified by baseline socio-demographic and clinical characteristics of patients on chronic HIV care at University of Gondar Referral Hospital, from October, 2006 to December, 2007.

Characteristics	No.of patients	Person-years	No.with TB	TB IDR (95%CI)	p-value
Total patients					
Age (years)					
15-29					
30-44					
≥ 45					
Sex					
Male					
Female					
Occupation					
Employed					
Unemployed					
Educational status					
Illiterate					
Literate					
Past History of TB					
Yes					
No					
Baseline CD4 cell count (cells/µl)					
<100					
≥100					
Baseline hemoglobin (gm/dl)					
<10					
≥10					
WHO stage					
Stage 1 or 2					
Stage 3 or 4					
IPT					
Yes					
No					
CPT					
Yes					
No					

TB, Tuberculosis ; IDR, Incidence density rate (per 100 person-years); CI, confidence interval; IPT, Isoniazid preventive therapy; CPT, Cotrimoxazole preventive therapy,

Table 2: Cox regression analysis of predictors of tuberculosis in HIV positive cohorts on chronic HIV care at University of Gondar Referral Hospital; from October, 2006- January, 2012

Variable	No. with TB	No. with no TB	Bivariate analysis		Multivariate analysis	
			CHR, (95%CI)	P-value	AHR, (95% CI)	P-value
Age (in years)						
15-29						
30-44						
≥45						
Sex						
Male						
Female						
Occupation						
Employed						
Unemployed						
Educational Status						
Illiterate						
Literate						
Baseline Hemoglobin (gm/dl)						
<10						
≥10						
Baseline CD4 cell count						
<100 cells/µl						
≥100 cells/µl						
WHO stage						
Stage 1 or 2						
Stage 3 or 4						
Past history of tuberculosis						
Yes						
No						
IPT						
Yes						
No						
CPT						
Yes						
No						
Adherence						
Good						
Fair						
Poor						

HR=Hazard ratio, **AHR**= adjusted hazard ratio; **CHR**=Crude hazard ratio, **CI**= Confidence interval
Note: All variables with a P-value of <0.2 in bivariate analyses will be included in multivariate analyses

Annex 4: Assurance of investigator

The undersigned senior MPH student agree to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research and publications office of the University of Gondar.

Student's Name: Kefyalew Addis Date: _____Signature: _____

Approval of the advisors:

Advisors' Name	Date	Signature
1. Belaynew wassie (MD,MPH)	_____	_____
2. Ansha Nega (RS, BSc, MSc)	_____	_____